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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/565,358	11/20/2006	Ashfaque Hossain	CRE-102.1 US (8492/96340)	5617

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EXAMINER	
BABIC, CHRISTOPHER M	

ART UNIT	PAPER NUMBER
1637	

MAIL DATE	DELIVERY MODE
12/21/2010	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/565,358	HOSSAIN ET AL.	
	Examiner	Art Unit	
	CHRISTOPHER M. BABIC	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 June 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-5,7 and 9-14* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5,7 and 9-14* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on June 11, 2010 has been entered. Claim(s) 1-5, 7, and 9-14 are pending and under examination.

Claim Rejections - 35 USC § 112 - Indefiniteness - New Grounds

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim(s) 1-5, 7, and 9-14 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The phrase "an affective amount" renders the metes and bounds of the claim indefinite because it is unclear what range of amounts constitutes an

"effective" amount and a person of skill in the art would not be reasonably apprised of the scope of the phrase.

The phrase is not defined by the claim or specification. This creates an issue with regard to scope because it is unclear what the term "effective" is specifically referencing. In other words, it is not clear if the amount is required to be effective to for example simply cause cell wall disruption; or for example, an amount effective to simply perform the method to isolate any yield of RNA from a biological specimen. There is no direction in the specification to what is considered "effective" and what is not.

Claim Rejections - 35 USC § 112 - New Matter - New Grounds

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim(s) 1-5, 7, and 9-14 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement.

The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Specifically, the limitation reciting, "an effective amount", added in

Applicant's response dated June 11, 2010, was not contemplated in the disclosure at the time the application was filed, and thus, is new matter.

Applicant does not point to any section of the disclosure as providing support for this amendment. Furthermore, a cursory review of the specification text did not reveal one instance of the phrase "effective amount." Thus, the phrase is not expressly defined by the claim or specification.

This creates an issue with regard to new matter because it is not clear that Applicant contemplated an "effective amount" at the time of filing. In other words, it is not clear if the amount is required to be effective to for example simply cause cell wall disruption; or for example, an amount effective to simply perform the method to isolate any yield of RNA from a biological specimen. There is no direction in the specification to what is considered "effective" and what is not.

Claim Rejections - 35 USC § 103 - Maintained

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary.

Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-5, 7, and 9-14 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Cook et al. (J Clin Microbiol. 2000 Dec;38(12):4326-31) in view of Chomczynski (U.S. 5,346,994), and in further view of Majumdar et al. (Biotechniques. 1991 Jul;11(1):94-101).

With regard to claims 1-3 and 8-14, Cook teaches methods of RNA isolation from biological specimens (pg. 4327, methods, col. 1, for example). Specifically, the reference teaches methods (pg. 4327, col. 1, RNA extraction from whole blood, for example) comprising: (a) contacting the biological specimen with an admixture of (i) "an effective amount of" mono-phasic solution of phenol and guanidine isothiocyanate (pg. 4327, col. 1, RNA extraction from whole blood, 2nd solution, TRIZOL solution necessarily contains phenol and guanidine isothiocyanate, for example), and (ii) "an effective amount of" lysis buffer under conditions and for a time appropriate to form a homogenate (pg. 4327, col. 1, RNA extraction from whole blood, 1st solution, CATRIMOX solution necessarily contains a dispersing agent, i.e. detergent, for example); (b) admixing the homogenate with a water-immiscible organic solvent under

conditions and for a time appropriate to form an aqueous phase and an organic phase (pg. 4327, col. 1, RNA extraction from whole blood, RNA was extracted by manufacture's instructions, for example); (c) contacting the aqueous phase with a C_1-C_4 lower alcohol under conditions and for a time to form a precipitated RNA (pg. 4327, col. 1, RNA extraction from whole blood, RNA was extracted by manufacture's instructions, for example); and (d) recovering the precipitated RNA (pg. 4327, col. 1, RNA extraction from whole blood, RNA was extracted by manufacture's instructions, for example).

With regard to the "admixture" of solutions (i) and (ii), Cook expressly teaches that the CATRIMOX-TRIZOL method was performed on some samples without the two DEPC water washes (pg. 4327, col. 1, RNA extraction from whole blood, for example). Thus within these methods, a CALTRIMOX residue was present in the reaction vessel during the addition of TRIZOL reagent.

With regard to the "manufacturer's instructions" referenced by Cook (pg. 4327, TRIZOL from Life Technologies, reference 5, for example), the Office believes it is understood that such instructions included the steps of: 1) forming aqueous/organic phases; and 2) RNA precipitation w/ isopropanol to isolate RNA from the TRIZOL homogenate, as such steps were considered standard in the art at the time of invention; however, in order to provide a clear understanding of the grounds of rejection, the Chomczynski reference is provided to demonstrate such method steps as standard methodology within RNA TRIZOL-based isolation at the time of invention (see Chomcynski; col. 5-6, Example 2, chloroform and isopropanol, for example).

With regard to the newly added language reciting "an effective amount," as discussed above, it is unclear what is in fact an "effective" amount. For the purposes of prior art application, the phrase is broadly interpreted to encompass amounts sufficient to complete the claimed purpose of the method, i.e. isolation of RNA, for any yield of RNA, from any bacterium specimen. In the instant case, an amount of CALTRIMOX, albeit a relatively small amount, was present in the reaction vessel during the addition of TRIZOL reagent. As Cook demonstrates, such an admixture of CALTRIMOX-TRIZOL was effective to isolate RNA from a biological sample.

With regard to the above claims, the CATRIMOX lysis buffer referenced by Cook does not appear to comprise a chelating agent (e.g. EDTA) as required by the claimed invention. Also, Cook does not teach RNA isolation from bacterium.

Majumdar provides a supportive disclosure that expressly teaches methods of bacterial RNA isolation that include an initial homogenization step that utilizes a lysis buffer comprising a dispersing agent (e.g. detergent) and a chelating agent (e.g. EDTA) (abstract; pg. 96-97, lysis of bacterial cells, TRITON-X100 and EDTA, for example). The reference expressly teaches EDTA as an essential reagent (pg. 99, col. 2), further highlighting that the simple extraction methods are useful for obtaining good yields from large and small samples (pg. 100, col. 3). It is submitted that referring to EDTA as an essential reagent would not have been surprising to one of ordinary skill in the art at the time of invention

given that EDTA was commonly known as a metal complexing agent, free metal ion activity being undesirable within isolated RNA solutions.

With regard to claims 4, 5, and 7, Majumdar teaches mammalian and *C. vibrioforme* samples (pg. 96-97, for example).

Thus, in summary, it is first submitted that it would have been *prima facie* obvious to one of ordinary skill in the art at the time of invention to apply the RNA isolation methods of Cook to bacteria since Mehra recognized that detergents were appropriate lysis reagents for bacterial nucleic acid isolation methods.

Furthermore, it would have been *prima facie* obvious to one of ordinary skill in the art at the time of invention to utilize steps (b) and (c) of the claimed method as demonstrated by Chomczynski in the methods of Cook since the prior art expressly demonstrates such steps as standard practice within TRIZOL-based isolation methods.

Furthermore, it would have been *prima facie* obvious to one of ordinary skill in the art at the time of invention to include a chelating agent (e.g. EDTA) within the lysis buffer of Cook since the prior art expressly demonstrates such a chemical as essential to providing good RNA yield. One of ordinary skill in the art would recognize the benefit of including such a chemical so as to form metal complexes thereby reducing free metal ion activity.

Response to Arguments

Applicant's arguments have been fully considered but they are not persuasive.

As argued previously, Applicant submits that application of one method to the extraction of RNA from whole blood does not suggest at a similar method could successfully be used for the extraction of RNA from bacterium. The examiner respectfully disagrees. As noted above, Mehra expressly teaches a detergent-based lysis procedure, i.e. application of a detergent (Triton) for the purpose of disrupting bacteria cellular structure. Thus, one of ordinary skill in the art would have expected caltrimox, a detergent, to be an appropriate lysis reagent for bacterial nucleic acid isolation.

Applicant provides no evidence of a probative value to support the above assertion. Applicant is respectfully reminded that the arguments of counsel cannot take the place of evidence in the record. In re Schulze, 346 F.2d 600, 602, 145 USPQ 716, 718 (CCPA 1965). Examples of attorney statements which are not evidence and which must be supported by an appropriate affidavit or declaration include statements regarding unexpected results, commercial success, solution of a long-felt need, inoperability of the prior art, invention before the date of the reference, and allegations that the author(s) of the prior art derived the disclosed subject matter from the applicant (see MPEP 716.01). Applicant is invited to contact the examiner to discuss any of the above issues.

Thus, the rejection is maintained.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christopher M. Babic whose telephone number is 814-880-9945. The examiner can normally be reached on Monday-Friday 10:00AM to 6:00PM EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 571-272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Christopher M. Babic/
Primary Examiner
Art Unit 1637

Technology Center 1600